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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/678,953	10/03/2000	Hiroshi Kubota	320727.50401.	7343

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KATTEN MUCHIN ZAVIS  
525 West Monroe Street  
Suite 600  
Chicago, IL 60661-3693

EXAMINER

TON, THAIAN N

ART UNIT PAPER NUMBER

1632

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

S.M.

**Office Action Summary****Application No.**

09/678,953

**Applicant(s)**

KUBOTA ET AL.

**Examiner**

Thai-An N Ton

**Art Unit**

1632

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 February 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicants' Amendment, filed 7/30/03 has been entered. Claims 1 and 14 have been amended. Claims 1-24 are pending. Claims 21-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11 (Filed 12/4/01).

Claims 1-20 are under current examination.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The prior rejection of claims 14-20 is withdrawn.

Claims 1 and 14 are vague and indefinite. The claims recite that the composition comprises isolated *single-cell* bipotent hepatic progenitors. It is unclear what the term "single-cell" encompasses and the specification fails to provide a definition for the term. For example, the term could mean a single bipotent hepatic progenitor cell in a composition of other cells. Claims 2-13 and 15-20 depend from claims 1 and 14, respectively.

#### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sargiacomo *et al.* [J. of Hepatology, 28:480-490, 1998], as further evidenced by Haruna [cited in the prior Office action].

The claims are directed to compositions comprising isolated single-cell bipotent hepatic progenitor cells which express at least one ICAM antigen and do not express MHC class 1a antigen, wherein the bipotent hepatic progenitors have the capacity to differentiate when exposed to differentiation-inducing growth conditions.

Note that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Further, it is noted that, "Products of identical chemical composition can not have mutually exclusive properties." A chemical

composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Applicants argue that Sargiacomo fails to teach the claimed invention because fundamental to Sargiacomo's method is that intact "multi-size spherical fetal liver culture system which allows morphogenetic hepatic units" were seeded into culture medium, to begin the growth process, so that hepatic architecture would be present. Applicants argue that Sargiacomo teaches at pages 480-481 that the use of intact, 3-dimensional cell clusters is a cure to deficiencies noted in the art of maintaining isolated hepatocytes in cell culture where the method includes "dissociation of cells from the tissue matrix in which reciprocal interactions are critical for the maintenance of a differentiated cellular state" (sentence bridging the argument that the cell clusters of Sargiacomo contain bipotent hepatic progenitors, pages 480-481). Applicants further argue that that Sargiacomo not only fails to teach the isolation of single-cell hepatic progenitors, but actually teaches away from single-cell culture methods. See pp. 9-10, bridging ¶ of the Response.

This is not found to be persuasive. The claims as amended require that the composition comprise isolated single-cell bipotent hepatic progenitors. As such, any composition with hepatic progenitor cells would consist of single cells of hepatic progenitor cells. Thus, the art, as taught by Sargiacomo anticipates the claimed

invention because the cell clusters would be made up of "single-cell" bipotent hepatic progenitors, as required by the claims. Furthermore, it is noted that Sargiacomo teaches control cultures, wherein the fetal liver cells were counted as monocellular suspensions, which would also comprise of single cells. See p. 481, col. 2, 1<sup>st</sup> full ¶, lines 7-10.

Applicants argue that Sargiacomo does not even indicate that bipotent hepatic progenitors exist within the cell cultures taught by Sargiacomo. Applicants argue that the Final Office Action would suggest that Sargiacomo's cell preparation must inherently contain bipotent hepatic progenitors as described by Applicants, it is also possible that the bipotent progenitors are excluded from Sargiacomo's cell preparation in the early stages. See p. 10 of the Response.

Applicants' arguments have not found to be persuasive. The claims are directed to products, in particular, compositions of single-cell bipotent hepatic progenitors. Thus, Sargiacomo's teaching of cultures of human fetal liver cells, with the evidence provided by Haruna, who identify bipotent progenitor cells in fetal human livers, wherein the time frame of isolation of the fetal livers overlap, would inherently contain bipotent hepatic progenitor cells.

Applicants argue that because Haruna teach the immunoperoxidase staining of formalin-fixed paraffin sections of intact liver, and thus, it would not be possible to determine if the cells as taught by Haruna would be present in the Sargiacomo cell preparation. Further, Applicants argue that Haruna's identification methods to the

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cultures of Sargiacomo would not yield the bipotent hepatic progenitor cells of the instant invention because Haruna's cells are no longer viable, thus no longer have the capacity to differentiate. See pp. 10-11 of the Response.

This is not found to be persuasive. Firstly, the cells as taught by Sargiacomo are obtained from intact fetal livers, dissociated and then seeded. See p. 481, Experimental Procedures. Thus, the cell preparations would contain all the cells that an intact fetal liver would contain. Thus, Haruna provides evidence of bipotent progenitor cells in a human fetal liver. As Sargiacomo's cells are disclosed to be isolated from human fetal livers, as are those cells claimed by Applicant, as well as those from Haruna, the cells would reasonably be expected to have the same physical and biochemical properties. As stated in the preceding paragraphs, a chemical composition and its properties are inseparable.

Accordingly, Sargiacomo *et al.* anticipate the claimed invention.

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*Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Note: After January 13, 2004, the Examiner may be reached at (571) 272-0736. If the Examiner is unavailable, inquiries may be directed to Deborah Reynolds, SPE of Art Unit 1632, at (571) 272-0734.

TNT  
THÁI-AN N. TON  
PATENT EXAMINER  
GROUP 1632

*Deborah Crouch*  
DEBORAH CROUCH  
PRIMARY EXAMINER  
GROUP 1600-7(1632)